

**WEST**☐ **Generate Collection****Print**

L10: Entry 2 of 3

File: DWPI

Jan 9, 1992

DERWENT-ACC-NO: 1992-060696  
DERWENT-WEEK: 200051  
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TITLE: Artificial blood comprising haemoglobin-including liposome - with polyethylene glycol bound hydrogenated natural phospho-lipid

PRIORITY-DATA: 1990JP-0107946 (April 24, 1990)

## PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
JP 04005242 A	January 9, 1992		000	
JP 3085963 B2	September 11, 2000		006	A61K038/16

INT-CL (IPC): A61K 9/08; A61K 9/12; A61K 9/127; A61K 9/50; A61K 37/14; A61K 38/16; A61K 47/14; A61K 47/34; A61K 47/36; A61P 7/08

ABSTRACTED-PUB-NO: JP 04005242A

## BASIC-ABSTRACT:

Artificial blood comprises modified haemoglobin-including liposome upon which an aggregation inhibitor, having a hydrophobic polymer moiety on one end and a hydrophilic polymer moiety on the other, is fixed. The inhibitor has hydrophobic end to the membrane surface so that the polymer is oriented with the hydrophilic end stretching outward from the surface. The liposome is suspended in aq soln of artificial plasma comprising water-sol. polymers.

The aggregation inhibitor is a polyethylene glycol-bound hydrogenated natural phospholipid. The av mol wt of the water-sol polymer is 20,000-70,000. The water-sol polymer is hydroxyethyl starch. The crystalline osmotic pressure of the artificial blood is acceptably adjusted to that of the living body to when it is administered. The colloidal osmotic pressure of the artificial blood is adjusted to that of the living body to when it is administered. The compsn of electrolytes is the same as that of the plasma. The compsn of the electrolytes is the same as that of Ringer soln, lactic acid Ringer soln or Crebs-Ringers soln.

USE/ADVANTAGE - The artificial blood is used as artificially adjusted oxygen-carrying infusions in lifesaving therapy for patients with massive bleeding. Low viscosity of the artificial blood resulting from the action of aggregation inhibitors renders easy the administration to living bodies without the fear of clogging by aggregates in blood capillaries. Also, the extremely low toxicity can realise its massive administration with safety.

In an example, a mixt of hydrogenated soybean lecithin, cholesterol, and myristic acid in CH<sub>2</sub>Cl<sub>2</sub> was concd, 50% hemoglobin aq soln (1000 ml) was added. The resulting liposome (av particle size 0.2 micron) was suspended in saline (10% hemoglobin concn). To this was added saline contg 5% polyethylene glycol-bound hydrogenated soybean lecithin and the resulting liposome was re-suspended in 6% hydroxyethyl starch aq saline (av mol wt 30,000-40,000, 10% hemoglobin

L Number	Hits	Search Text	DB	Time stamp
1	23	tsuchida-eishun-.in.	USPAT; US-PGPUB	2003/10/08 11:18
2	4	sakai-hiromi-.in.	USPAT; US-PGPUB	2003/10/08 11:18
3	1	tomiyama-kenichi-.in.	USPAT; US-PGPUB	2003/10/08 11:18
4	8	takeoka-shinji-.in.	USPAT; US-PGPUB	2003/10/08 11:19
5	2	sou-keitaro-.in.	USPAT; US-PGPUB	2003/10/08 11:20
6	3384	oxygen same (hemoglobin or haemoglobin or hb)	USPAT; US-PGPUB	2003/10/08 11:20
7	585	((oxygen same (hemoglobin or haemoglobin or hb)) same deoxy\$10	USPAT; US-PGPUB	2003/10/08 11:20
8	5	((oxygen same (hemoglobin or haemoglobin or hb)) same deoxy\$10) same (polyoxyethylene or (polyethylene adj glycol))	USPAT; US-PGPUB	2003/10/08 11:27
9	186	((oxygen same (hemoglobin or haemoglobin or hb)) same (vesicle\$1 or infusion\$1)	USPAT; US-PGPUB	2003/10/08 11:27
10	46	((oxygen same (hemoglobin or haemoglobin or hb)) same (vesicle\$1 or infusion\$1)) same (lipid\$1 or liposome\$1)	USPAT; US-PGPUB	2003/10/08 11:27
11	1	((oxygen same (hemoglobin or haemoglobin or hb)) same (vesicle\$1 or infusion\$1)) same (lipid\$1 or liposome\$1) same deoxy\$10	USPAT; US-PGPUB	2003/10/08 11:32
12	1	((oxygen same (hemoglobin or haemoglobin or hb)) same (vesicle\$1 or infusion\$1)) same (lipid\$1 or liposome\$1) same (polyoxyethylene or (polyethylene adj glycol))	USPAT; US-PGPUB	2003/10/08 11:28
13	20	((oxygen same (hemoglobin or haemoglobin or hb)) same (vesicle\$1 or infusion\$1)) same (lipid\$1 or liposome\$1) and (polyoxyethylene or (polyethylene adj glycol))	USPAT; US-PGPUB	2003/10/08 11:28
14	29	((oxygen same (hemoglobin or haemoglobin or hb)) same (vesicle\$1 or infusion\$1)) same (lipid\$1 or liposome\$1) and deoxy\$10	USPAT; US-PGPUB	2003/10/08 11:32
15	13	((oxygen same (hemoglobin or haemoglobin or hb)) same (vesicle\$1 or infusion\$1)) same (lipid\$1 or liposome\$1) and deoxy\$10) not (((oxygen same (hemoglobin or haemoglobin or hb)) same (vesicle\$1 or infusion\$1)) same (lipid\$1 or liposome\$1) and (polyoxyethylene or (polyethylene adj glycol)))	USPAT; US-PGPUB	2003/10/08 11:35
16	1	4911929.pn.	USPAT; US-PGPUB	2003/10/08 11:35
17	1	4776991.pn.	USPAT; US-PGPUB	2003/10/08 11:35
18	1	6054427.pn.	USPAT; US-PGPUB	2003/10/08 11:36
19	1	6054427.pn. and deoxy\$10	USPAT; US-PGPUB	2003/10/08 11:38
20	1	5985825.pn.	USPAT; US-PGPUB	2003/10/08 11:38
21	1	5814601.pn.	USPAT; US-PGPUB	2003/10/08 11:39
22	1187068	n-(monomethoxypolyoxyethylene adj carbamyl)	USPAT; US-PGPUB	2003/10/08 11:40
23	3	((n-(monomethoxypolyoxyethylene adj carbamyl)) near2 (distearoyl adj phosphatidyl-ethanolamine)	USPAT; US-PGPUB	2003/10/08 11:41

d his

(FILE 'HOME' ENTERED AT 09:21:52 ON 08 OCT 2003)

FILE 'CAPLUS, CAOLD, MEDLINE, BIOSIS' ENTERED AT 09:22:32 ON 08 OCT 2003  
E TSUCHIDA EISHUN/AU

L1 1205 S E3  
L2 360 S L1 AND OXYGEN  
L3 26 S L2 AND DEOXY?  
L4 3 S L3 AND POLYOXYETHYLENE  
L5 3 DUP REMOV L4 (0 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 09:27:04 ON 08 OCT 2003

FILE 'CAPLUS, CAOLD, MEDLINE, BIOSIS' ENTERED AT 09:28:01 ON 08 OCT 2003

L6 1 S L3 AND POLYETHYLENE GLYCOL  
E SAKAI HIROMI/AU  
L7 136 S E3  
L8 82 S L7 AND OXYGEN  
L9 14 S L8 AND DEOXY?  
L10 2 S L9 AND (POLYOXYETHYLENE OR POLYETHYLENE GLYCOL)  
E TOMIYAMA KENICHI/AU  
L11 11 S E3  
L12 7 S L11 AND OXYGEN  
L13 2 S L12 AND DEOXY?  
E TAKEIKA SHINJI/AU  
E TAKEOKA SHINJI/AU  
L14 210 S E3  
L15 89 S L14 AND OXYGEN  
L16 13 S L15 AND DEOXY?  
L17 2 S L16 AND (POLYOXYETHYLENE OR POLYETHYLENE GLYCOL)  
E SOU KEITARO/AU  
L18 16 S E3  
L19 6 S L18 AND OXYGEN  
L20 4 S L19 AND DEOXY?  
L21 3 DUP REMOV L20 (1 DUPLICATE REMOVED)

FILE 'STNGUIDE' ENTERED AT 09:32:34 ON 08 OCT 2003

FILE 'CAPLUS, CAOLD, MEDLINE, BIOSIS' ENTERED AT 09:33:32 ON 08 OCT 2003


L22 29161 S OXYGEN AND (HEMOGLOBIN OR HAEMOGLOBIN OR HB)  
L23 3382 S L22 AND DEOXY?  
L24 43 S L23 AND (POLYOXYETHYLENE OR POLYETHYLENE GLYCOL)  
L25 2 S L24 AND (VESICLE? OR INFUSION?)

FILE 'STNGUIDE' ENTERED AT 09:48:22 ON 08 OCT 2003

FILE 'CAPLUS, CAOLD, MEDLINE, BIOSIS' ENTERED AT 10:20:35 ON 08 OCT 2003

L26 3 S L24 AND (INERT OR NITROGEN)  
L27 3 DUP REMOV L26 (0 DUPLICATES REMOVED)  
L28 41 S L24 NOT L25  
L29 39 S L28 NOT L27  
L30 19 DUP REMOV L29 (20 DUPLICATES REMOVED)  
L31 0 S MONOMETHOXYPOLYOXYETHYLENE CARBAMYL DISTEAROYL PHOSPHATIDYL E

L21 ANSWER 2 OF 3 CAPLUS COPYRIGHT.2003 ACS on STN DUPLICATE 1  
AN 2000:254323 CAPLUS  
DN 133:125017  
TI Poly(ethylene glycol)-Conjugation and **Deoxygenation** Enable  
Long-Term Preservation of Hemoglobin-Vesicles as **Oxygen** Carriers  
in a Liquid State  
AU Sakai, Hiromi; Tomiyama, Ken-ichi; **Sou, Keitaro**; Takeoka,  
Shinji; Tsuchida, Eishun  
CS Department of Polymer Chemistry Advanced Research Institute for Science  
and Engineering, Waseda University, Tokyo, 169-8555, Japan  
SO Bioconjugate Chemistry (2000), 11(3), 425-432  
CODEN: BCCHES; ISSN: 1043-1802  
PB American Chemical Society  
DT Journal  
LA English  
RE.CNT 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT



L25 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2003 ACS on STN

AN 2000:422159 CAPLUS

DN 133:155212

TI Characteristics and function of human **hemoglobin vesicles** as an **oxygen** carrier

AU Ogata, Yoshitaka

CS Terumo Corp. R and D Center, Kanagawa, 259-01, Japan

SO Polymers for Advanced Technologies (2000), 11(5), 205-209

CODEN: PADTE5; ISSN: 1042-7147

PB John Wiley & Sons Ltd.

DT Journal

LA English

AB A liposome-encapsulated human **Hb** (NRC) was developed and evaluated as an artificial **oxygen** carrier. The NRC is a liposome-encapsulated highly concd. (>45%) stroma-free human **Hb** with inositol hexaphosphate (IHP as an allosteric effector), a coenzyme and substrates for reducing methHb (methHb). The NRC surface was coated with **polyethylene glycol** to prevent aggregation in plasma and to prolong their retention time in the blood stream. The **oxygen** binding behavior of the NRC in vitro was investigated and it was found that it effectively transports **oxygen** in vivo as an **oxygen** carrier. The **oxygen** binding behavior and kinetics were studied by the stopped-flow method and the **oxygen** binding curve of the NRC was detd. The **oxygen** binding speed and binding coeff. (Kon) of NRC, washed human red blood cells (WRBC) and stroma-free human **Hb** (SFHb) were measured by stopped-flow method. The **oxygen** binding speed of SFHb was the highest, while that of RBC was the lowest and that of NRC was intermediate. The **oxygen** binding of NRC ended within 60 ms when **deoxy**-NRC was mixed with **oxygen**. The Kon of NRC was 2.9 .times. 10<sup>5</sup>, 10-fold faster than that of RBC. The **oxygen** binding curve and P5002 of NRC that contained various IHP concns. were measured. The **oxygen**-binding curve of the NRC sequentially shifted to the right as the IHP content was increased. Exchange transfusion of 70% was carried out for rats with NRC contg. various concns. of IHP and of **Hb**, and investigated the optimum concn. of NRC in vivo. The lactate value after exchange transfusion was 3-fold higher than before exchange transfusion, when rats were subjected to exchange transfused with NRC that did not contain IHP. But the increase of lactate was suppressed when rats were transfused with NRC that contained IHP. When the **Hb** concn. of NRC was 5 and 6%, exchange transfused rats recovered to normality just like rats transfused with RBC.

RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

# WEST Search History

DATE: Wednesday, October 08, 2003

<u>Set Name</u> side by side	<u>Query</u>	<u>Hit</u> <u>Count</u>	<u>Set</u> <u>Name</u> result set
<i>DB=JPAB,EPAB,DWPI,TDBD; PLUR=YES; OP=ADJ</i>			
L12	L11 not l10	9	L12
L11	l9 and (liposome\$1 or lipid\$1)	11	L11
L10	L9 and (polyoxyethylene or (polyethylene adj glycol))	3	L10
L9	l6 and (vesicle\$1 or infusion\$1)	31	L9
L8	L7 and (polyoxyethylene or (polyethylene adj glycol))	2	L8
L7	L6 and deoxy\$10	72	L7
L6	oxygen and (hemoglobin or haemoglobin or hb)	926	L6
L5	sou-k-\$.in.	0	L5
L4	takeoka-s-\$.in.	1	L4
L3	tomivama-k-\$.in	0	L3

L2 sakai-h-\$.in.

0 L2

L1 tsuchida-e-\$.in.

0 L1

END OF SEARCH HISTORY